Craig (C. F.)

NOTES ON THE PATHOLOGY AND BACTERIOLOGY OF APPENDICITIS.

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Member of the American Medical Association, American Microscopical Society, Conn. State Medical Society, Fairfield Co. Medical Society, Pathologist to the Danbury Medical Society.

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IT IS my purpose in this paper to record the pathological and bacteriological findings in a series of diseased appendices submitted to me for examination. Before doing so, however, it may not be uninteresting to consider the normal histology of the appendix vermiformis as but few writers have given us any exact or comprehensive account of its normal structure. It is situated at the lower and back part of the cæcum, communicating with it by an orifice which, according to Gray, is sometimes guarded by an incomplete valve. The appendix extends upward and inward behind the cæcum, coiled upon itself and ending in a blunt point, being held in place by a peritoneal fold, which may form a mesentery for it. In two hundred dissections of this organ made by Ferguson, of Toronto, the appendix had its own mesentery in one hundred and twenty-three instances. Its normal length is given by Gray as from three to six inches, the diameter of its canal being about equal to that of a goose quill. In its histological structure it resembles the large intestine, being composed of four coats, serous, muscular, sub-mucous and mucous.

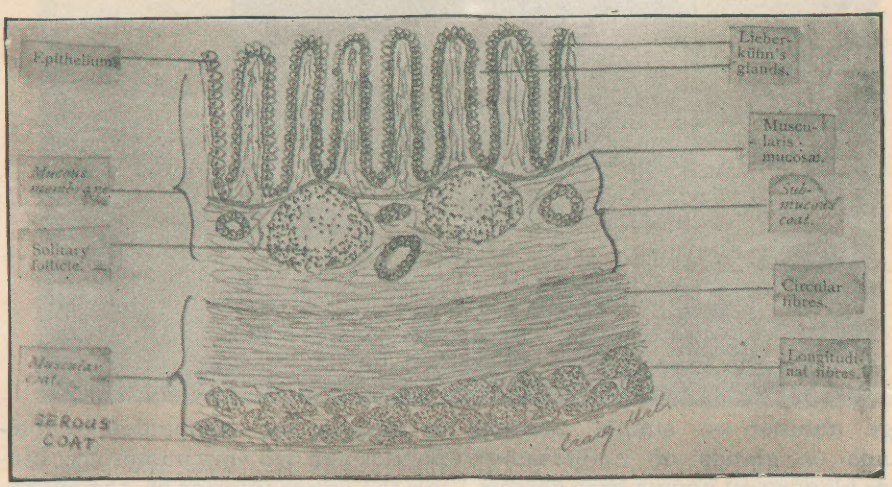

Fig. 1.

Diagram of a transverse section of the normal appendix. This drawing is intended to show the various histological layers.

The serous coat, or more accurately speaking, the peritoneal, is the outermost coat and is composed of a very thin layer of fibrous tissue covered upon its outer surface by a layer of endothelial cells.

The muscular coat is composed of an external layer of longitudinal fibres and an internal layer of circular fibres. In the sections examined by me the external longitudinal layer is divided into three narrow bands, separated sometimes by a little areo-

lar tissue but generally so closely united as to be almost indistinguishable. The longitudinal layer of fibres is much thinner than the circular layer which is thick and strong. The submucous coat is normally thin and composed of very loose connective tissue which supports the blood vessels, lymphatics and nerves. It serves also to connect the circular muscular coat to the mucous coat.

The mucous coat, or mucosa, is the most interesting from a pathological standpoint, as it is here that the first changes take place in disease of the appendix. It is devoid of villi and Peyer's patches as is the large intestine generally, but consists of a base of adenoid tissue supporting a large number of simple tubular glands or glands of Leiberkuhn; these glands rest upon a very narrow muscular layer called the muscularis mucosæ. This was not always distinguishable in my sections.

The appendix also contains in this layer, a large number of the so-called solitary glands.

The adenoid tissue which supports the tubular glands is filled with leucocytes.

Imbedded in the adenoid tissue lie the tubular glands, each consisting of a delicate membrane lined by a row of columnar epithelium which is continuous with that lining the mucous membrane. The tubular glands in the appendix are much longer than the similar glands in the small intestine. The closed ends of these glands reach nearly to the muscularis mucosæ, which forms a muscular band composed of longitudinal and circular fibres. The solitary glands or follicles are masses of adenoid tissue generally oval in shape and filled with leucocytes; their lower border projects into the sub-mucous layer, while their apices lie in the mucous layer, being covered by the tubular glands and the epithelium lining the appendix. The leucocytes which these glands contain were often seen in my sections, to have invaded the tissue lying between the tubular glands and to have accumulated at their orifices. These solitary glands or follicles are surrounded by lymphatics and are very numerous. Lining the entire interior of the appendix is a layer of epithelium continuous with that lining the tubular glands.

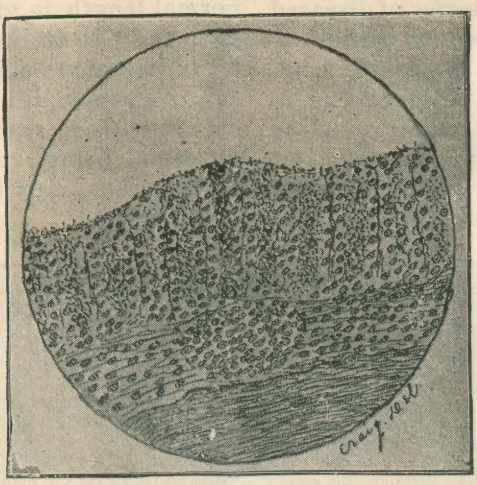

Fig. 2.

Section through mucous, sub-mucous and muscular coats of appendix, showing infiltration of glands, interglandular tissue and sub-mucous tissue with leucocytes. At the center of the section is a solitary gland. Here and there may be seen groups of bacteria.
Objective, 1-5 in., eye-piece, 1¼ in.

To recapitulate, then, the structure of the appendix from without inward is briefly as follows: (See Fig. 1.)

1. A peritoneal investment or serous coat.

2. A muscular coat, composed of longitudinal and circular fibres.

3. A sub-mucous coat, composed of connective tissue supporting blood vessels, lymphatics and nerves.

4. A mucous coat, composed of a narrow layer of muscular fibres, the muscularis mucosæ, which supports

a mass of adenoid tissue, in which are imbedded the tubular glands or glands of Leiberkuhn and the solitary glands or follicles.

Having considered the normal histology of the appendix we will now take up its pathological histology.

All inflammations of the appendix may be divided into the following classes, as given by Deaver, i. e: catarrhal, ulcerative, perforative, an advanced stage of ulcerative, tubercular and recurrent. The pathological changes met with vary from those of a simple inflammation with a limited invasion of the tissue by leucocytes, to pus formation, ulceration and necrosis of the entire wall in places and consequently perforation. The specimens examined by me embrace all the stages mentioned, from the slightly inflamed appendix containing no pus, up to the necrosed and perforated appendix filled with purulent exudation. Of the appendices examined one showed little or no inflammation, two were inflamed but showed no perforation, and the remaining five contained more or less pus, and were perforated in one or more places.

Beside the pathological examination, a careful bacteriological study was made of each case, cultures being made and microscopical specimens stained. I shall first give the pathological and conclude with the bacteriological data.

Appendix No. 1.—Case of Dr. E. A. Stratton. This appendix was removed from a man 65 years old, who had had one attack of appendicitis in February of this year. In June he was again taken sick but with symptoms which were not those of a straight appendicitis. An operation was performed in thirty-six hours after the beginning of the attack, and a pus centre was found in the intestine, the appendix being apparently normal.

It was about three inches long, of normal diameter, and with a permeable canal. The extremity was, how-

Fig. 3.

Section of diseased appendix. This shows the first stages of inflammation, the mucous layer being much thickened in places, and infiltrated with leucocytes, the glandular structure being but partly destroyed. The light oval patch beneath the glands, near the center of the picture, is a solitary follicle. Taken with a ¾ in. objective, 1½ in. eye-piece. Wide angle lens.

ever, a little enlarged and tumefied. The organ was hardened and imbedded in paraffine, and a large number of sections made. This specimen is of great interest as it proved to be in normal condition near the base, while inflammatory process had begun at the extremity. Within one inch of the base, the appendix presented a normal histological appearance, but as the sections approached the extremity a pathological change is seen to have taken place, first evidenced by a thickening and projection of the mucous layer. This is noticeable even in sections examined by the naked eye. The thickening is due to an invasion of the adenoid tissue and inter-glandular tissue by countless numbers of leucocytes, (Fig. 2) which have rallied to the aid of the organism in overcoming the action of some irritant, either physical, chemical, or bacterial. At this stage the tissue between the glands is filled with leucocytes, as are also the glands themselves, and the adenoid tissue lying beneath them. The lumen of the canal is still open, though slightly contracted.

In sections taken nearly at the enlarged extremity, the change in the mucous membrane is much more pronounced, the mucosa and adenoid tissue being so enlarged as to nearly obliterate the canal of the appendix (Fig. 3) a further change at this period is the thickening of the sub-mucous coat, which normally is less in width than the combined muscular and peritoneal coats, but which has increased so that it is nearly half again as thick as both combined. This increased thickness is due to invasion by leucocytes and multiplication of the connective tissue cells. The appearance of a section of the appendix at this stage of inflammation is as follows, beginning from within outwards. The tubular glands and inter-glandular tissue is crowded with innumerable leucocytes, the gland structure being in some places destroyed; the adenoid tissue is increased in amount and thickened, infiltrated with leucocytes, while the solitary glands imbedded in it are immensely distended by leucocytes. The sub-mucous tissue is increased in amount and pretty well infiltrated; the circular muscular coat is well preserved but there is here and there a deposit of leucocytes; the longitudinal muscular coat and the

Fig. 4.

Section of diseased appendix. This photograph shows only the immensely thickened mucous layer, which has almost entirely closed the canal. The gland structure is shown, as well as masses of exudation at the mouths of the glands, and filling the canal. The entire mucous membrane is densely infiltrated with leucocytes.
Taken with a ¾ in. objective, 1½ in. eye-piece. Wide angle lens.

serous coat are normal. (Figs. 4, 5, 6).

Sections taken at the extremity of the appendix show simply an exaggeration of the condition described, the mucous layer being so increased as to entirely close the lumen of the canal; there is a dense infiltration of leucocytes, the sub-mucous layer is greatly increased in width, the circular and longitudinal muscular coats are thinly infiltrated, and the serous coat is normal. In this appendix, then, we have evidence of an inflammation commencing at the mucous layer of the organ and gradually working its way outward toward the peritoneal investment, the first changes taking place in the epithelium lining the simple glands, the tissue becoming infiltrated by leucocytes which have been brought up by Nature to repair the injury, but the enemy penetrating still further, causes an invasion of the adenoid, the sub-mucous, and the muscular coats. There has as yet been no great destruction of the tissue, but the protecting epithelial covering of the glandular lining of the appendix has been pierced, thus allowing the casual agent access to the underlying tissue which is rich in lymphatics and blood vessels.

It is evident that some irritating agent has been at work and that this agent came from within the appendix. Unfortunately, I did not secure this specimen until it had been in alcohol for some days, so that it was impossible for cultures to be made, but from the reports to follow, it is very probable that the cause would have been found to have been bacterial in nature. The sections from this appendix are of great interest as they show the condition present, probably in the very first stages of the disease. It is the condition present before there has been much exudation and before the formation of pus.

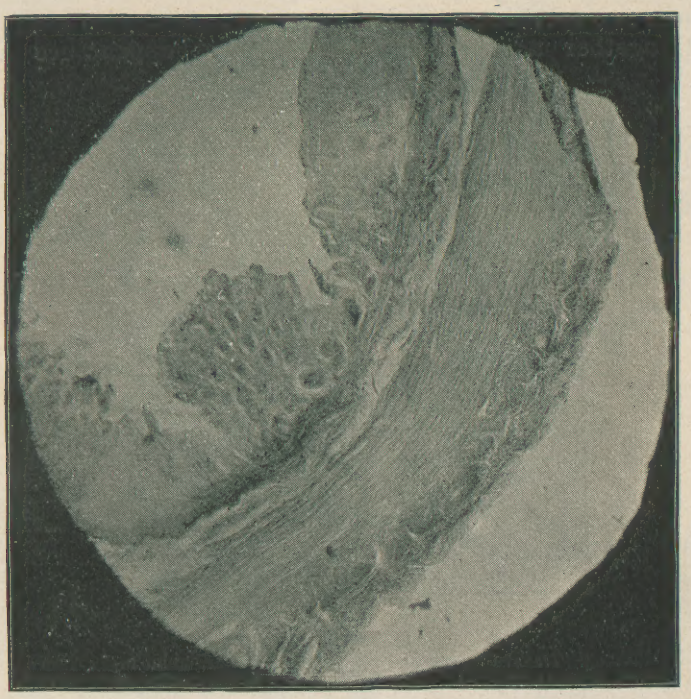

Fig. 5.

Section of diseased appendix. Just to the left of the centre of the photograph the appendix is normal, while at the right may be seen the infiltration of the mucous layer by leucocytes, which has obliterated the glands. The sub-mucous and muscular coats are, as yet, normal.
Taken with a ¾ in. objective, 1½ in. eye-piece. Wide angle lens.

Appendix No. 2.—Case of Dr. C. P. Bennett. Young man, aged 18, had had previous attacks of colic. Was taken with severe pain at midnight and first seen at 4 A. M. Typical symptoms of appendicitis were present and operation was advised and performed within 48 hours after this visit. On opening into the abdomen the appendix was found coiled upon itself and inflamed. It was removed and was found enlarged and tume-

fied, but perforation had not taken place.

Appendix No 3.—Case of Dr. D. C. Brown. Girl, aged 19, had had three previous attacks, the last in June of this year. She was operated on in the interval. The appendix was found bound down by numerous adhesions as was also the cæcum. The appendix was removed together with a large mass of inflammatory tissue which surrounded the gut and which necessitated the application of a number of ligatures. The organ was greatly enlarged and showed areas of ulceration. (Fig. 7).

The pathological changes encountered in these two specimens may be considered together as they were very similar. It may be said that the condition present was an advanced stage of that described in appendix No. 1, the inflammatory process having gone on to pus formation and ulceration, but not to perforation. The mucous layers are enormously thickened in places, projecting markedly into the canal, but on account of the destruction of the glandular and adenoid tissue, the canal remains patent. The submucous coat is thickened and the muscular coats somewhat thinned. At intervals, in the sections, can be seen places where the mucous and submucous layers are entirely destroyed, leaving the circular muscular coat exposed, constituting minute ulcers, which would ultimately have perforated the muscular coats. Like the first case described, there is found here the same infiltration with leucocytes of the various layers, most numerous in the mucous and submucous layers, but also very numerous in the muscular coats. (Fig. 8). The areas of ulceration or necrosis are bounded by the still undestroyed glands and adenoid tissue, their floor being formed by the smooth circular muscular coat, destruction of the mucous and sub-mucous layers having taken place.

Various staining methods were employed to detect bacteria, and in sections stained with methyl blue an interesting appearance was presented. It was found that the mucous layer was literally loaded with bacteria, which had penetrated into and between the glands, and invaded the adenoid tissue, and less markedly the muscular layer. (Fig. 2). A microscopic examination of a section thus stained will demonstrate this fact, for it can be seen that the glandular and a portion of the adenoid tissue are stained very much more deeply than the remainder of the section, owing to the fact that the great masses of bacteria take the stain much more rapidly than the rest of the tissue.

The pathological changes found at this stage of inflammation show that the irritating agent is capable of

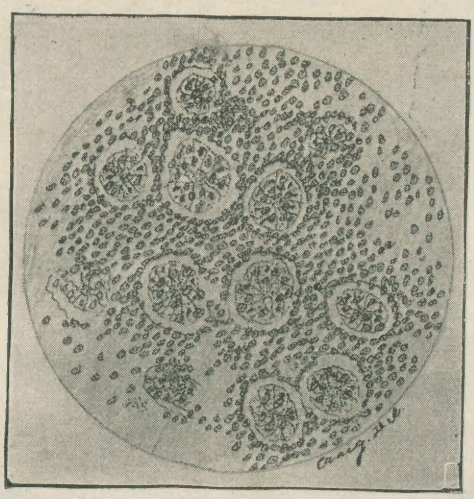

Fig. 6.
Transverse section of the tubular glands, in an inflamed appendix. The inter-glandular tissue, as well as the gland structure, is packed with leucocytes.
Objective, 1·5 in., eye-piece, 1½ in.

causing the destruction of the mucous and sub-mucous coats of the appendix and from the evidence presented we have the right to infer that the irritating agent is a micro-organism.

Appendix No. 4.—Case of Dr. W. S. Watson. A boy, aged 13 years was taken sick on Friday with severe pain in the left iliac region. Medical attendance was not sought until the following Tuesday, when an appendicitis upon the left side was diagnosed but on account of the bad condition of the patient operation was postponed until the next day. Just before operation the boy died, and upon post-mortem it was found that there was a transposition of all the abdominal organs as well as the heart; the appendix lay upon the left side, bathed in pus and held down by adhesions. It was very extensively inflamed and the canal filled with exudation; about the middle of the canal there was a small necrotic area, and near the extremity a large perforation. The canal also contained a fecal concretion.

Appendix No. 5.—Case of Dr. W. S. Watson. A boy, six years old, first attack, was operated upon the day after first seen, appendicitis having been diagnosed. The appendix was found to have ruptured, the abdomen containing much pus. The organ was removed and was found to be intensely inflamed and showed a perforation at the extremity. The canal was filled with exudation, but there was no necrotic areas save where perforation had taken place.

Appendix No. 6.—Case of Dr. C. P. Bennett. A young man, aged 20, had had three attacks previously, the last in the preceding summer. When first seen there were present typical symptoms of appendicitis accompanied by a severe bronchitis. Temperature was 100.5. Operation was advised and performed next day. An hour before operation the temperature rose suddenly to 105, with symptoms of rupture. At the operation the abdomen was found full of serous pus, and the appendix plastered firmly to the cæcum along its entire length, with a small perforation at its extremity. It was removed and found to be enlarged, distended with exudation and perforated.

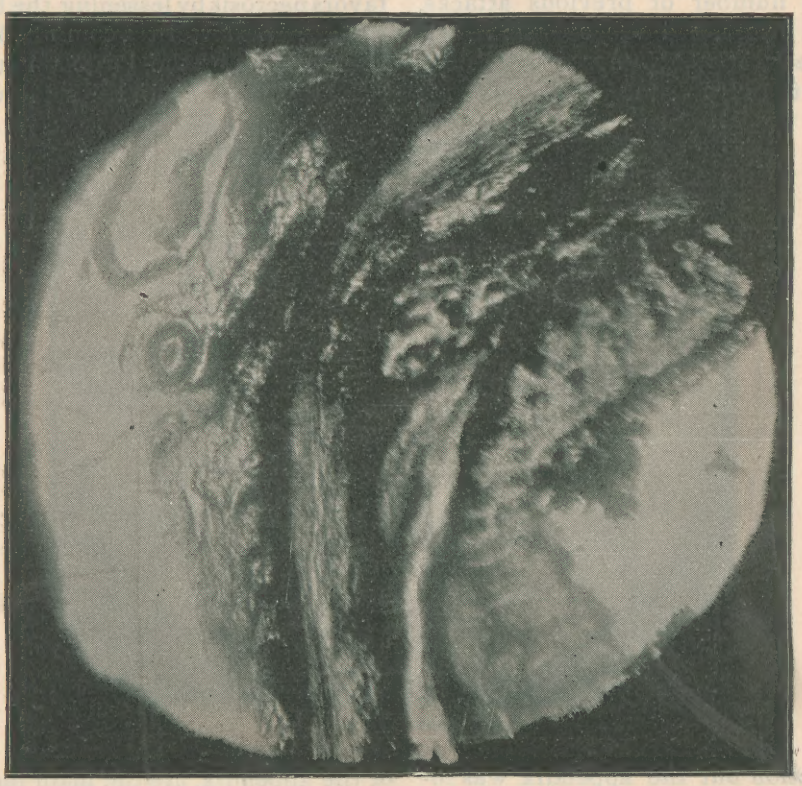

Fig. 7.

Section of diseased appendix, showing the greatly thickened mucous and sub-mucous layers, the thinned muscular layers and endarteritis of the artery. At one portion may be seen an area of destruction of the tissue between the mucous and sub-mucous coats.
Taken with ¾in. objective, 1½ in. eye-piece. Wide angle lens.

Appendix No. 7.— Case of Dr. E. A. Stratton. A young man, aged 19, had typical symptoms of appendicitis and operation was performed 48 hours after first visit. The abdomen contained pus which was free in the cavity, no abscess wall being discovered. The appendix was removed and found to be inflamed along its entire length, tumefied and containing two areas of necrosis, one about its middle, the other near the extremity where there was a perforation.

Appendix No. 8.—Case of Dr. E. A. Stratton. Italian, male, had had a large number of previous attacks, eight or ten, and was operated upon in the interval. Numerous adhesions were found which necessitated much dissection but the appendix was located and removed. It was greatly inflamed and perforation had taken place about its lower third. It contained much purulent matter.

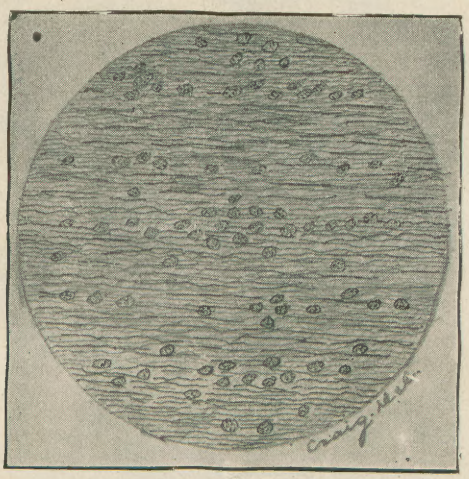

Fig. 8.

Section of the muscular coat of inflamed appendix. This section shows the infiltration of the muscular coat by leucocytes.
Objective, 1-5 in., eye-piece 1½ in.

The microscopic pathology of the cases just given may be considered as a whole, as in all of them the appearances presented are similar, the disease having ended in necrosis and perforation. (Figs. 9, 10). The mucous and sub-mucous layers are much increased in thickness in some places, and densely infiltrated with leucocytes, while in others these layers have almost entirely disappeared, leaving the muscular coat exposed. Where necrosis has occurred but the process has not extended further than the muscular coats, the mucous and sub-mucous layers are seen to consist, in places, of merely a framework of disintegrated tissue, all structure having disappeared. Where perforation has taken place we see the entire wall of the appendix eaten through, the tissue around the perforation being necrosed. Another change which has been spoken of, but which is far more noticeable at this stage, is the thinning of the muscular coat, evidently due to compression by the exudation. In some of the sections endarteritis of the artery of the appendix is observed, which favors necrosis by lessening the blood supply. Endarteritis, combined with compression by the large amount of exudation shut up in the small canal of the appendix, are the main factors in the production of necrosis. All the layers of the appendix at this final stage are packed with leucocytes, and this is true of even those portions farthest removed from the necrotic areas. The solitary glands or follicles are entirely disintegrated, being composed of masses of leucocytes and broken down tissue.

Bacteriological Examination.—The method of making cultures from the specimens was as follows: The appendix was cut open with a knife heated to a red heat, and a platinum needle, previously heated, was drawn over the surface of the canal of the appendix and the tube inoculated and placed in the incubator.

Appendix No. 1.—No cultures made.

Appendix No. 2.—3.—In all the tubes inoculated from this specimen there appeared a pure culture of the bacillus coli communis. These cultures were grown through several generations and were carefully examined and identified. The growth in all the tubes was luxuriant.

In the tubes inoculated from appendix No. 3, there occurred a mixed growth composed of the bacillus coli communis and staphylococcus pyogenes aureus. These organisms were separated and pure cultures secured of each.

communis and the pneumococcus. The occurrence of pneumococci in this case is of much interest, as the boy died on the fifth day of pneumonia. When first seen he had a severe bronchitis complicating the appendicitis and it is very possible that the rise of temperature to 105° shortly before operation was due in part to the commencing pneumonia. The finding of pneumococci in the appendix would certainly point to this, and is not at all at variance with the well known characteristics of the organism, as it has been found in a

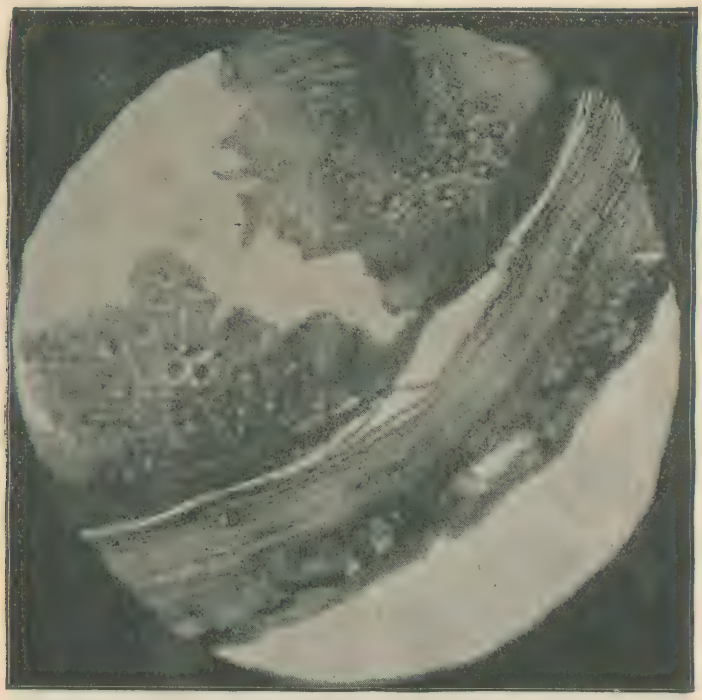

Fig. 9.

Section of diseased appendix, showing an area of necrosis, thickened mucous layer, which on the right is undergoing destruction, the glandular structure being obliterated by a dense infiltration of leucocytes. The entire mucous, submucous and muscular coats are packed with leucocytes, which gives the granular appearance to the picture.
Taken with a ¾ in. objective, 1½ in. eye-piece. Wide angle lens.

Appendix No. 4.—Cultures were made upon agar-agar and gelatine and a mixed growth was obtained, which on separation was found to consist of the bacillus coli communis and the streptococcus pyogenes.

Appendix No. 5.—Cultures were made upon agar-agar and gelatine and resulted in a pure growth of the bacillus coli communis.

Appendix No. 6.—Cultures were made upon agar-agar and gelatine and resulted in a mixed growth. The organisms present were separated and found to be the bacillus coli

variety of conditions and diffused widely through the system; after experimental inoculation of these germs into susceptible animals all the internal organs have been found to contain them as well as the blood vessels and lymphatics. It is my belief that pneumonia had developed in this case before operation.

Appendix No. 7.—Cultures were made upon agar-agar and gelatine and resulted in pure growths of the bacillus coli communis.

Appendix No. 8.—Cultures were made upon the same media and re-

sulted in a mixed growth. The organisms were separated and found to be the bacillus coli communis and the staphylococcus pyogenes. It will be seen that in the cases examined the bacillus coli communis was found to be present three times in pure culture, twice in conjunction with the staphylococcus pyogenes aureus, once with the streptococcus pyogenes and once with the pneumococcus. The relation of this bacillus to appendicitis is at present the subject of much attention, some authorities claiming that it is the cause while by others it is considered of little or no importance. This germ is normally present in the intestine and has been found by Hodenpyl in the normal appendix. It has been proven by many observers, notably Abbott, Green, Welch, Barbacci, Malvoz and A. Fraenkel, that it is also present in a great variety of diseased conditions, and that it is capable of producing grave pathological changes. Inoculations of animals with pure cultures of this germ always results in a spreading inflammation, abscess formation, and often septic poisoning, just the phenomena we have in appendicitis, but from the fact that it is present in the normal appendix and does not cause trouble, we are justified in believing that there must be some other factor to be accounted for. It has been shown that the virulence of the bacillus coli communis is intensified if the intestinal membrane is injured, and that it can only enter the system when such an injury is present, and Cumston, in an article upon the virulence of this organism in the intestinal diarrhœas of infants found that it is always greater than when it is in the intestine of the healthy child. Given, then, an organism whose virulence is increaeds when its habitat is in any way injured, we can understand how the bacillus coli communis may be the chief agent in the production of appendicitis. The interior of the appendix is lined by a layer of epithelium which resists the passage of bacteria. If, however, the delicate cells which compose this layer, be injured in any way, as by stricture, the presence of a fecal mass, a sudden strain, etc., the resulting leak in the membrane of defense will permit of the passage of the bacillus into the underlying tissue, which is rich in lymphatics, thus forming an ideal

Fig. 10.

Ulcer of the appendix. Necrosis of the mucous and submucous coats has taken place, the circular muscular coat being exposed, and forming the floor of the ulcer. Taken with ¾ in. objective, 1½ in. eye piece. Wide angle lens.

surface for general infection of the appendix. The bacillus coli communis, aroused to increased virulence by this injury to its native heath, seizes the opportunity and invades and poisons the exposed tissue. Of course any other germs which may be present would also be liable to enter the breach, and produce their characteristic effects.

From my examinations, I would conclude then, that appendicitis is due generally to the invasion of the tissues of the appendix by bacteria, notably the bacillus coli communis, which invasion is made possible by the destruction, in some way, of the guarding layer of epithelium. I can see, however, how a purely mechanical cause such as a foreign body, might, by continued irritation, cause an exudation which being confined in the small canal of the appendix might, by compression, cause necrosis and perforation, without the aid of bacteria, but I believe that in the vast majority of cases the bacillus coli communis is the chief factor in the etiology of the disease.

Briefly stated then, the pathology of appendicitis may be summed up as follows:

1. An injury to the delicate epithelium lining the interior of the appendix, and which constitutes its protective barrier.

2. The invasion of the mucous membrane and sub-mucous tissue, rich in lymphatics and blood vessels, by bacteria, chiefly the bacillus coli communis.

3. The infiltration of these layers by leucocytes, which have rallied to repel the invasion, and consequently swelling of the mucous and sub-mucous layers, with some exudation.

4. The invasion of the muscular coat by bacteria and leucocytes, with destruction of the mucous and sub-mucous layers, and the formation of areas of necrosis and ulceration, due to pressure, impaired blood supply and microbial poisons.

Lastly, the entire destruction, in parts, of the mucous, sub-mucous, muscular and serous coats, and consequently perforation of the appendix.

As to the primal causal factor, that which produces the lesion in the epithelium, I believe that there is more than one. Any mechanical, chemical or bacterial agency capable of injuring this delicate tissue, may be concerned. I do not believe that the primal cause is often bacterial, but after such injury has occurred I believe the pathological changes which then begin are due to the invasion of the rich lymphatic tissue by bacteria, the chief of which is the bacillus coli communis.